

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

- For more records, click the Records link at page end.
- To change the format of selected records, select format and click Display Selected.
- To print/save clean copies of selected records from browser click Print/Save Selected.
- To have records sent as hardcopy or via email, click Send Results.

<input type="checkbox"/> <b>Select All</b>	<input checked="" type="checkbox"/> <b>Print/Save Selected</b>	<input type="checkbox"/> <b>Send Results</b>	<b>Format</b>
<input checked="" type="checkbox"/> <b>Clear Selections</b>			<input checked="" type="checkbox"/> <b>Display Selected:</b> <b>Full</b> <input checked="" type="checkbox"/>

1.  8/19/1

010866107

WPI Acc No: 1996-363058/199637

Related WPI Acc No: 1995-015667; 1998-242391

XRAM Acc No: C96-114414

XRPX Acc No: N96-306047

Gut sutures which can be dry packaged - coated with  
bioabsorbable copolymer composed mainly of epsilon-caprolactone and also  
of copolymerisable monomer(s), in presence of polyhydric alcohol  
initiator

Patent Assignee: US SURGICAL CORP (USSU )

Inventor: BENNETT S L; JIANG Y; ROBY M S; TOTAKURA N

Number of Countries: 007 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
CA 2162801	A	19960515	CA 2162801	A	19951114	199637 B
<u>EP 774265</u>	A1	19970521	EP 95118169	A	19951117	199725 N
US 5939191	A	19990817	US 9375995	A	19930611	199939
			US 94338668	A	19941114	
			US 96657059	A	19960528	
			US 97880303	A	19970623	

Priority Applications (No Type Date): US 94338668 A 19941114; EP 95118169 A 19951117; US 9375995 A 19930611; US 96657059 A 19960528; US 97880303 A 19970623

Cited Patents: 00 12804300; 00 62858700; 03 89681400; 04 20121600; 5037429

Patent Details:

Patent No	Kind	Lan Pg	Main IPC	Filing Notes
-----------	------	--------	----------	--------------

CA 2162801	A	18	A61M-017/00	
------------	---	----	-------------	--

EP 774265	A1	E	9 A61L-017/00	
-----------	----	---	---------------	--

Designated States (Regional): DE ES FR GB IT

US 5939191	A.	B05D-001/36	CIP of application US 9375995
------------	----	-------------	-------------------------------

Cont of application US 94338668
---------------------------------

Cont of application US 96657059
---------------------------------

Abstract (Basic): CA 2162801 A

Gut sutures are coated with a compsn. comprising a bioabsorbable copolymer made from a major amt. of epsilon -caprolactone and a minor amt. of at least one other copolymerisable monomer, in the presence of polyhydric alcohol as initiator. Opt. the suture can be precoated.

Pref. the other copolymerisable monomer is selected from glycolide, lactide, p-dioxanone and trimethylene carbonate. The polyhydric alcohol is in amt. 0.5-5 (pref. 0.1-2) wt.% and is selected from glycerol, trimethylolpropane, 1,2,4-butanetriol, 1,2,6-hexanetriol, triethanolamine, tri-isopropanolamine, erythritol, threitol, pentaerythritol, ribitol, arabinitol, xylitol, N,N,N',N'-tetrakis(2-hydroxyethyl)ethylenediamine, N,N,N',N'-tetrakis(2-hydroxypropyl)ethylenediamine, dipentaerythritol, allitol, dulcitol, glucitol, altritol, iditol, sorbitol, mannitol and inositol. Epsilon-caprolactone is in amt. 70-98 (pref. 80-95) wt.%.

USE - The sutures are useful in conventional surgery.

**ADVANTAGE** - The coated gut sutures can be packaged dry i.e. without tubing fluid, so can be used as soon as the package is opened. However they remain flexible and fray resistant.

Dwg.0/0

Title Terms: GUT; SUTURE; CAN; DRY; PACKAGE; COATING; BIO; ABSORB; COPOLYMER; COMPOSE; MAINLY; EPSILON; CAPROLACTONE; COPOLYMERISE; MONOMER; PRESENCE; POLY; HYDRIC; ALCOHOL; INITIATE

Derwent Class: A23; A25; A96; D22; E19; G02; P31; P34; P42

International Patent Class (Main): A61L-017/00; A61M-017/00; B05D-001/36

International Patent Class (Additional): A61B-017/04

File Segment: CPI; EngPI

Manual Codes (CPI/A-N): A02-A; A05-E02; A09-A07; A10-D03; A12-V03; D09-D; E10-A07; E10-B01D; E10-E04H; E10-E04J; G02-A05

Chemical Fragment Codes (M3):

- \*01\* H4 H402 H403 H404 H405 H482 H483 H484 H8 M280 M311 M312 M313 M314 M315 M316 M321 M322 M323 M331 M332 M333 M340 M342 M343 M344 M383 M391 M392 M393 M416 M620 M781 M903 M904 Q121 Q261 Q332 9637-A0201-U
- \*02\* H1 H103 H182 H4 H404 H484 H8 M280 M312 M323 M332 M342 M383 M393 M416 M620 M781 M903 M904 Q121 Q261 Q332 9637-A0202-U
- \*03\* H4 H405 H484 H8 K0 L8 L818 L821 L833 M280 M315 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 Q121 Q261 Q332 R09008-U
- \*04\* H4 H403 H483 H8 M280 M314 M321 M332 M343 M383 M391 M416 M620 M781 M903 M904 Q121 Q261 Q332 R16534-U
- \*05\* H4 H405 H484 H5 H581 H8 M280 M315 M322 M334 M344 M383 M392 M416 M620 M781 M903 M904 Q121 Q261 Q332 R13512-U
- \*06\* H4 H404 H484 H8 K0 L8 L818 L821 L833 M280 M314 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R01168-U
- \*07\* H4 H403 H483 H8 M280 M313 M321 M332 M343 M383 M391 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R00113-U
- \*08\* G036 G563 H4 H403 H463 H8 M280 M320 M415 M510 M520 M530 M541 M781 M903 M904 Q121 Q261 Q332 R07555-U
- \*09\* H4 H405 H484 H8 K0 L8 L818 L821 L833 M280 M315 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 Q121 Q261 Q332 R09009-U
- \*10\* H4 H405 H484 H8 K0 L8 L816 L821 L833 M280 M315 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R00290-U
- \*11\* H4 H404 H484 H8 M280 M315 M321 M334 M344 M383 M391 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R00972-U
- \*12\* H4 H405 H484 H8 K0 L8 L812 L821 L833 M280 M315 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 Q121 Q261 Q332 R10994-U
- \*13\* H4 H405 H484 H8 K0 L8 L814 L821 L833 M280 M315 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R00032-U
- \*14\* H4 H404 H484 H8 K0 L8 L818 L821 L833 M280 M314 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 Q121 Q261 Q332 R10762-U
- \*15\* H1 H103 H181 H4 H403 H483 H8 M280 M312 M323 M332 M342 M383 M393 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R00743-U
- \*16\* H1 H103 H181 H4 H403 H483 H8 M280 M313 M323 M331 M342 M383 M393 M416 M620 M781 M903 M904 Q121 Q261 Q332 R08669-U
- \*17\* H4 H403 H483 H8 M280 M315 M321 M333 M343 M383 M391 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R00420-U
- \*18\* H4 H405 H484 H8 K0 L8 L818 L821 L833 M280 M315 M321 M332 M344 M383 M391 M416 M620 M781 M903 M904 M910 Q121 Q261 Q332 R00545-U

Polymer Indexing (PS):

<01>

- \*001\* 018; R24034 G3714 P0599 D01 F70; S9999 S1070-R
- \*002\* 018; K9610 K9483; B9999 B5436 B5414 B5403 B5276; B9999 B5447 B5414 B5403 B5276; K9687 K9676; N9999 N7090 N7034 N7023; ND01; K9574 K9483; K9698 K9676; Q9999 Q8059 Q7987; N9999 N7147 N7034 N7023; B9999 B4035 B3930 B3838 B3747; N9999 N7045 N7034 N7023; B9999 B4080 B3930 B3838 B3747; B9999 B4171 B4091 B3838 B3747; B9999 B3907 B3838

B3747

&lt;02&gt;

- \*001\* 018; H0022 H0011; R01295 G2131 D01 D23 D22 D31 D42 D50 D77 D86 F43; G4068 G2131 D01 D10 D11 D22 D23 D32 D46 D50 D76 D86 F43; P0055; M9999 M2153-R; M9999 M2186; L9999 L2528 L2506; L9999 L2186-R; L9999 L2744 L2733; L9999 L2391; L9999 L2153-R; S9999 S1605-R; S9999 S1627 S1605; P1978-R P0839 D01 D50 D63 F41
- \*002\* 018; H0022 H0011; R01295 G2131 D01 D23 D22 D31 D42 D50 D77 D86 F43; R17298 G2131 D01 D23 D22 D31 D46 D50 D84 F43; P0055; M9999 M2153-R; M9999 M2186; L9999 L2528 L2506; L9999 L2186-R; L9999 L2744 L2733; L9999 L2391; L9999 L2153-R; S9999 S1605-R; S9999 S1627 S1605; P1978-R P0839 D01 D50 D63 F41
- \*003\* 018; H0022 H0011; R01295 G2131 D01 D23 D22 D31 D42 D50 D77 D86 F43; G1638 G1592 D01 D22 F34 G2142 G2131 F43 D23 D31 D76 D46 D50 D84; P0055; M9999 M2153-R; M9999 M2186; L9999 L2528 L2506; L9999 L2186-R; L9999 L2744 L2733; L9999 L2391; L9999 L2153-R; S9999 S1605-R; S9999 S1627 S1605; L2200
- \*004\* 018; H0022 H0011; R01295 G2131 D01 D23 D22 D31 D42 D50 D77 D86 F43; G1309 G1296 D01 D63 F44 D23 D22 D31 D76 D46 D50 D84; P0055; M9999 M2153-R; M9999 M2186; L9999 L2528 L2506; L9999 L2186-R; L9999 L2744 L2733; L9999 L2391; L9999 L2153-R; S9999 S1605-R; S9999 S1627 S1605; H0260; P0839-R F41 D01 D63; P0862 P0839 F41 F44 D01 D63
- \*005\* 018; R01295 G2131 D01 D23 D22 D31 D42 D50 D77 D86 F43; G4068 G2131 D01 D10 D11 D22 D23 D32 D46 D50 D76 D86 F43; R17298 G2131 D01 D23 D22 D31 D46 D50 D84 F43; G1638 G1592 D01 D22 F34 G2142 G2131 F43 D23 D31 D76 D46 D50 D84; G1309 G1296 D01 D63 F44 D23 D22 D31 D76 D46 D50 D84; H0033 H0011; P0055; M9999 M2153-R; M9999 M2186; L9999 L2528 L2506; L9999 L2186-R; L9999 L2744 L2733; L9999 L2391; L9999 L2153-R; S9999 S1605-R; S9999 S1627 S1605; P1978-R P0839 D01 D50 D63 F41; P0953 P0839 P0964 H0260 F34 F41 D01 D63; L9999 L2200; H0260; P0839-R F41 D01 D63; P0862 P0839 F41 F44 D01 D63
- \*006\* 018; ND06; K9518 K9483; K9610 K9483; K9687 K9676; K9712 K9676; Q9999 Q7114-R; B9999 B3021 B3010; B9999 B3678 B3554; B9999 B5094 B4977 B4740; N9999 N6780-R N6655; N9999 N6860 N6655; ND01; K9574 K9483; K9698 K9676; Q9999 Q8059 Q7987; N9999 N7147 N7034 N7023; B9999 B4035 B3930 B3838 B3747; N9999 N7045 N7034 N7023; B9999 B4080 B3930 B3838 B3747; B9999 B4171 B4091 B3838 B3747; B9999 B3907 B3838 B3747
- \*007\* 018; D01 D11 D10 D50 D84 D85 D86 F29 F26; R00113 G1070 G0997 D01 D11 D10 D50 D83 F29 F26; R00420 G1070 G0997 D01 D11 D10 D50 D86 F29 F26; R00743 G2153 D01 D11 D10 D50 D86 F08 F07 F29 F26; R00972 G1070 G0997 D01 D11 D10 D50 D85 F29 F26; R00032 G1070 G0997 D01 D11 D10 D50 D86 F29 F26; D01 D14 D13 D31 D76 D50 D86 F29 F26; D01 D11 D10 D50 D89 F08 F07 F29 F26; D01 D11 D10 D50 D90 D93 F09 F07 F29 F26; D01 D11 D10 D50 D90 F29 F26 F34; H0226
- \*008\* 018; R05350 D01 D11 D10 D50 D61 D93 F36 F35 Sn 4A; C999 C102 C000; C999 C306; C999 C328
- \*009\* 018; R00862 D01 D02 D11 D10 D19 D18 D31 D50 D76 D87; A999 A475

&lt;03&gt;

- \*001\* 018; R00351 G1558 D01 D23 D22 D31 D42 D50 D73 D82 F47; H0000; P0055; P8004 P0975 P0964 D01 D10 D11 D50 D82 F34; M9999 M2153-R; M9999 M2200; S9999 S1627 S1605
- \*002\* 018; R00370 G1558 D01 D11 D10 D23 D22 D31 D42 D50 D73 D83 F47; H0000; P0055; P8015 P0975 P0964 D01 D10 D11 D50 D83 F34
- \*003\* 018; K9518 K9483; B9999 B5447 B5414 B5403 B5276; Q9999 Q7114-R; B9999 B5094 B4977 B4740; N9999 N7090 N7034 N7023; B9999 B3554-R; ND01; K9574 K9483; K9698 K9676; Q9999 Q8059 Q7987; N9999 N7147 N7034 N7023; B9999 B4035 B3930 B3838 B3747; N9999 N7045 N7034 N7023

; B9999 B4080 B3930 B3838 B3747; B9999 B4171 B4091 B3838 B3747;  
B9999 B3907 B3838 B3747  
\*004\* 018; R00271 D01 D11 D10 D50 D83 F27 F26; A999 A475  
Derwent Registry Numbers: 0032-U; 0113-U; 0290-U; 0420-U; 0545-U; 0743-U;  
0972-U; 1168-U  
Specific Compound Numbers: R09008-U; R16534-U; R13512-U; R01168-U; R00113-U  
; R07555-U; R09009-U; R00290-U; R00972-U; R10994-U; R00032-U; R10762-U;  
R00743-U; R08669-U; R00420-U; R00545-U  
Generic Compound Numbers: 9637-A0201-U; 9637-A0202-U

Derwent WPI (Dialog® File 351); (c) 2002 Derwent Info Ltd. All rights reserved.

---

[Select All](#)     [Clear Selections](#)     [Print/Save Selected](#)     [Send Results](#)     [Display Selected](#)    **Format**  [Full](#)

© 2002 The Dialog Corporation plc

(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets

(11)



EP 0 774 265 A1

(12)

## EUROPEAN PATENT APPLICATION

(43) Date of publication:

21.05.1997 Bulletin 1997/21

(51) Int. Cl.<sup>6</sup>: A61L 17/00

(21) Application number: 95118169.2

(22) Date of filing: 17.11.1995

(84) Designated Contracting States:

DE ES FR GB IT

Jiang, Ying  
North Haven, CT 06473 (US)  
Bennett, Steven L.  
New Haven, CT 06513 (US)

(71) Applicant: United States Surgical Corporation  
Norwalk, Connecticut 06856 (US)

(74) Representative: Marsh, Roy David et al  
Hoffmann Eitle & Partner  
Patent- und Rechtsanwälte  
Arabellastrasse 4  
81925 München (DE)

(72) Inventors:

• Totakura, Nagabhushanam  
North Haven, CT 06473 (US)  
• Roby, Mark S.  
Killingworth, CT 06419 (US)

### (54) Coated gut suture

(57) A gut suture is coated with a bioabsorbable copolymer obtained by polymerizing a major amount of ε-caprolactone and a minor amount of at least one other copolymerizable monomer in the presence of polyhydric alcohol as initiator. The coated gut suture can be packaged in the absence of conventional tubing fluid, i.e., in the dry state, while at the same time retaining flexibility, pliability and resistance to fray. In an alternative embodiment, a gut suture is coated with a pre-coating composition prior to being coated with the bioabsorbable copolymer.

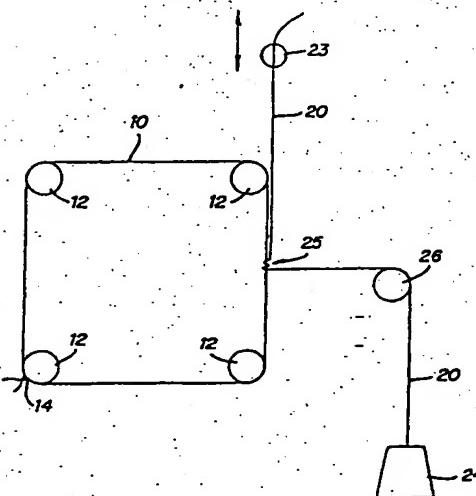


FIG. 1

EP 0 774 265 A1

DescriptionBACKGROUND5    1. Technical Field

The present disclosure relates to a coated gut suture and, more particularly, to a coated gut suture which is capable of being dry packaged.

10    2. Background of the Related Art

Absorbable sutures are manufactured from natural or synthetic materials. Some of the earliest absorbable sutures were made of collagenous material taken from sheep intestines. Such sutures are still in use today and are commonly referred to as "catgut" or simply "gut" sutures or ligatures. In the present specification, the term "catgut" or "gut" suture 15 refers to a collagen based suture or ligature of any type or origin. Gut sutures may be prepared in the form of threads or strands that are undesirably stiff before subsequent treatment which renders them flexible or pliable.

A suture having a good degree of flexibility and pliability can conform closely to body tissue without undue pressure. Good flexibility and pliability enhance the degree to which a suture can be tied down, knotted and securely placed in a desired position.

20    Various attempts have been made to modify and optimize the physical characteristics of gut sutures. For example, tubing fluids, i.e., liquids which are used to condition gut sutures to achieve or enhance flexibility and pliability, have been used to preserve gut sutures. Tubing fluids typically contain an alcohol such as isopropyl alcohol and a relatively small percentage of water. Examples of tubing fluids are found in U.S. Patent Nos. 1,239,690, 2,394,054, 2,519,404, 2,524,772, and 2,694,487. Ideally, the tubing fluid aids the gut suture to retain its flexibility and pliability without 25 adversely affecting the strength and overall integrity of the suture.

Commercially available gut sutures are immersed in tubing fluid, sterilized and supplied to surgeons in packages or tubes which contain tubing fluid. The alcohol and water present in the tubing fluid keep the suture flexible and pliable as long as they remain in contact with the suture. As the tubing fluid evaporates, the suture loses its flexibility and pliability which may affect handling characteristics.

30    In addition to tubing fluids, various suture coatings which adhere to the surface of the suture have been developed in an attempt to maintain flexibility and control swelling and fraying. Such coatings are also intended to improve the handling characteristics of sutures and maximize run-down performance. For example, U.S. Patent No. 3,942,532 discloses a suture coating composition obtained by polymerizing lactones such as  $\epsilon$ -caprolactone in the presence of a polymethylene diol. U.S. Patent No. 4,624,256 discloses a suture coating composition containing a high molecular weight  $\epsilon$ -caprolactone homopolymer, or a copolymer derived from a major amount of  $\epsilon$ -caprolactone and a minor amount of a comonomer or a blend of such an  $\epsilon$ -caprolactone polymer with a lubricating agent (e.g., sterol esters of fatty acids).

Copolymers derived from  $\epsilon$ -caprolactone and at least one other monomer such as glycolide, lactide, p-dioxanone and trimethylene carbonate are disclosed in U.S. Patent Nos. 4,605,730, 4,624,256, 4,700,704, 4,788,979, 4,791,929, 4,994,074, 5,076,807, 5,080,665, 5,085,629 and 5,100,433.

40    U.S. Patent No. 3,896,814 discloses a dry-packaged gut suture which is coated with a treatment agent such as polyoxyethylene glycol. U.S. Patent No. 4,027,676 discloses a gut suture coated with a three-component coating composition. This patent discloses polyalkylene glycol as one ingredient of the three-component coating composition. U.S. Patent No. 4,506,672 discloses a gut suture coated with a cured isocyanate-capped polyester which can be packaged either dry or in alcohol-containing wrappers. U.S. Patent No. 4,649,920 discloses an absorbable surgical suture coated 45 with a high molecular weight poly(alkylene oxide).

The aforementioned U.S. Patent Nos. 3,896,814, 4,027,676, 4,506,672 and 4,649,920 do not disclose a gut suture which is coated with an  $\epsilon$ -caprolactone-containing bioabsorbable copolymer.

SUMMARY

50    A gut suture is coated with a composition comprising a bioabsorbable copolymer obtained by polymerizing a major amount of  $\epsilon$ -caprolactone and a minor amount of at least one other copolymerizable monomer in the presence of a polyhydric alcohol initiator.

The use of a polyhydric alcohol initiator, i.e., an alcohol possessing three or more hydroxyl groups, provides a 55 copolymer having a branched, or "star", configuration. The branched structure of the bioabsorbable copolymer exerts a characteristic influence on its bioabsorption behavior making it useful as a coating material for gut sutures.

The gut suture coated with the bioabsorbable copolymer can optionally be packaged in the dry state, i.e., in the absence of tubing fluid, and yet still maintain substantially the same degree of flexibility, pliability and resistance to fray exhibited by a gut suture which is stored in tubing fluid. Thus, a gut suture coated with a coating composition in accord-

5. cance with this disclosure can be packaged in a manner which is typical for conventional surgical sutures and, when removed from its package, be immediately employed by the surgeon.

In an alternative embodiment, a pre-coating composition is applied to the gut suture prior to being coated with a bioabsorbable copolymer in accordance with this disclosure. A preferred pre-coating composition includes poly(alkylene oxide) such as polyethylene glycol.

#### BRIEF DESCRIPTION OF THE DRAWING

Fig. 1 schematically illustrates a fray testing system for sutures.

10

#### DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Conventional polymerization techniques that are well known and disclosed in the prior art can be utilized in preparing the bioabsorbable copolymer employed as a coating composition for a gut suture. The bioabsorbable copolymer is obtained by polymerizing a major amount of  $\epsilon$ -caprolactone and a minor amount of at least one other copolymerizable monomer or mixture of such monomers in the presence of a polyhydric alcohol initiator. The polymerization of these monomers contemplates all of the various types of monomer addition, i.e., simultaneous, sequential, simultaneous followed by sequential, sequential followed by simultaneous, etc.

Suitable monomers which can be copolymerized with  $\epsilon$ -caprolactone include glycolide, lactide, p-dioxanone and trimethylene carbonate.

Suitable polyhydric alcohol initiators include glycerol, trimethylolpropane, 1,2,4-butanetriol, 1,2,6-hexanetriol, triethanolamine, triisopropanolamine, erythritol, threitol, pentaerythritol, ribitol, arabinitol, xylitol, N,N,N',N'-tetrakis(2-hydroxyethyl)ethylenediamine, N,N,N',N'-tetrakis(2-hydroxypropyl)ethylenediamine, dipentaerythritol, allitol, dulcitol, glucitol, altritol, iditol, sorbitol, mannitol, inositol, and the like.

The copolymer can contain from about 70 to about 98, and preferably from about 80 to about 95, weight percent  $\epsilon$ -caprolactone-derived units, the balance of the copolymer being derived from the other copolymerizable monomer(s). The inherent viscosity of the copolymer generally ranges from about 0.10 to about 0.60, and preferably from about 0.20 to about 0.50, dl/g when measured in chloroform at a concentration of 0.2500 g/dl at 30°C. The polyhydric alcohol initiator is generally employed in small amounts, e.g., from about 0.5 to about 5, and preferably from about 0.1 to about 2, weight percent of the total monomer mixture.

The bioabsorbable copolymer can be applied to a gut suture by any suitable process, e.g., by passing the gut suture through a solution of the copolymer, e.g., in acetone, methylene chloride, etc., past a brush or other coating solution applicator, or past one or more spray nozzles dispensing the gut suture coating solution. The gut suture wetted with the coating solution is subsequently air dried and/or passed through or held in a drying oven for a time and at a temperature sufficient to vaporize and drive off the solvent. Preferably, the coated gut suture is first air dried and then dried in an oven maintained at a temperature of about 50°C. The solution of bioabsorbable copolymer can contain a suitable amount of water or other moisturizing agent which swells the gut suture and imparts a desirable degree of flexibility and pliability to the suture. The bioabsorbable copolymer will entrap the moisture within the suture and/or enhance the retention of the moisture within the suture. If desired, the gut suture coating composition can optionally contain additional components, e.g., dyes, antibiotics, antiseptics, growth factors, anti-inflammatory agents, etc. The amount of coating composition applied to a gut suture will vary depending upon the structure of the suture, e.g., the number of filaments, tightness of braid or twist, the size of the suture and its composition.

In an alternative embodiment herein, a gut suture is pre-coated with a pre-coating composition prior to being coated with the bioabsorbable copolymer disclosed herein. Examples of pre-coating compositions which can be employed herein include compositions containing fatty acids, esters and ethers of fatty acids, polyalcohols, fatty alcohols, glycerine, glycols and derivatives thereof and poly(alkylene oxides). Pre-coating compositions containing poly(alkylene oxides) are preferred. Particularly preferred are poly(alkylene oxides) or derivatives thereof having molecular weights ranging from about 300 to about 5000. Examples of poly(alkylene oxides) which can be employed include polyethylene glycol, polypropylene glycol and polyethylene glycol methyl ether. Such pre-coating compositions can generally be applied to the gut suture at a level of from about 0.1 to about 10 weight percent or more and preferably from about 0.5 to about 5 weight percent, based on the final weight of the coated gut suture. The pre-coating composition can be applied to a gut suture by simply immersing the suture in a solution or suspension containing the pre-coating composition and drying the suture. The solution or suspension can contain water which swells the gut suture and becomes entrapped therein by virtue of the coating of the pre-coating composition. Optionally, the gut suture can be immersed in water and/or moisturizing agent to render the suture flexible and pliable prior to contacting the suture with the solution/suspension containing pre-coating composition.

The bioabsorbable copolymer can be applied to the suture after application of the pre-coating composition. The amount of bioabsorbable copolymer applied to a gut suture which has been pre-coated can range from about 0.2 to as much as about 3 weight percent or more and preferably from about 0.5 to about 2 weight percent. For a gut suture which

has not been pre-coated, the bioabsorbable copolymer can be applied at a level of from about 0.5 to about 4 weight percent or more and preferably from about 1 to about 3 weight percent. As a practical matter, it is generally preferred to apply the minimum amount of coating composition consistent with good tie-down performance. This level of coating can be readily determined employing routine experimental procedures.

5 The following examples should be considered as illustrative and not as limitations of the present description. The examples demonstrate that coating formulations containing bioabsorbable copolymer and pre-coating composition as disclosed herein enhance the properties of gut sutures coated therewith.

Formulation 1

10 Dry glycolide (300g),  $\epsilon$ -caprolactone (2760g); stannous octoate as catalyst (0.3g) and dry mannitol as initiator (39.0g) were mixed under N<sub>2</sub> for one hour. The mixture was heated in a reactor at a temperature of 160°C for 24 hours. A solution of the resultant copolymer was prepared by dissolving the copolymer (5g) in toluene (95cc) and stirring the resultant mixture.

15 Formulation 2

A solution of polyethylene glycol methyl ether 350 (PEGME 350) (number average molecular weight of 350 and viscosity of 4.1 centistokes at 210°F) was prepared by mixing PEGME 350 (50cc) in isopropyl alcohol (50cc) and stirring the resultant mixture.

Formulation 3

20 A solution of polyethylene glycol methyl ether 350 was prepared by mixing PEGME 350 (as used in Formulation 2) (70cc) in isopropyl alcohol (30cc) and stirring the resultant mixture.

Formulation 4

25 A solution of polyethylene glycol methyl ether 350 was prepared by mixing 60 cc of PEGME 350 (as used in Formulation 2) with 40 cc of a solution made from 20% water and 80% isopropyl alcohol.

Formulation 5

30 A solution of polyethylene glycol 600 (PEG 600) (number average molecular weight of 600 and viscosity of 10.5 centistokes at 210°F) was prepared by mixing 60 cc of PEG 600 in 40 cc of a solution made from 20% water and 80% isopropyl alcohol.

EXAMPLE 1

40 Chrome gut sutures of size 1 are passed through a 10% solution of the copolymer of Formulation 1 in methylene chloride. The sutures are then air dried to remove the solvent, leaving a coating of the copolymer on the suture.

EXAMPLE 2

45 A chrome size 1 gut suture was dipped in the solution of Formulation 2 for 30 minutes, air dried and thereafter dried in an oven at 50°C for 5 minutes. The suture was then dipped in the solution of Formulation 1 for about 1 minute, air dried for 120 minutes and oven-dried at 50°C for 5 minutes. The resulting suture was then packaged dry and tested for number of cycles to break.

50 EXAMPLE 3

A chrome size 1 gut suture was dipped in the solution of Formulation 3 for 30 minutes, air dried and thereafter dried in an oven at 50°C for 5 minutes. The suture was then dipped in the solution of Formulation 1 for about 1 minute, air dried for 120 minutes and oven-dried at 50°C for 5 minutes. The resulting suture was then packaged dry and tested for number cycles to break.

EXAMPLE 4

A chrome size 1 gut suture was immersed in the solution of Formulation 4 for 30 minutes at 50°C, air dried for 60

minutes and thereafter immersed in the solution of Formulation 1 for about 1 minute. The suture was then removed, air dried for 120 minutes and oven-dried at 50°C for 5 minutes. The resulting suture was then packaged dry and tested for number of cycles to break.

5    EXAMPLE 5

A chrome size 1 gut suture was immersed in the solution of Formulation 5 for 30 minutes at 50°C, air dried for 60 minutes and thereafter immersed in the solution of Formulation 1 for about 1 minute. The suture was removed, air dried for 120 minutes and oven-dried at 50°C for 5 minutes. The resulting suture was then packaged dry and tested for 10 number of cycles to break.

COMPARATIVE EXAMPLE 1

A chrome size 1 gut suture was immersed in isopropyl alcohol for 30 minutes at 50°C, air dried for 60 minutes and 15 thereafter immersed in toluene for one minute. The coated suture was removed, air dried for 120 minutes and oven-dried at 50°C for 5 minutes. Thus, this gut suture contains no polymeric coating composition. The suture was packaged dry and tested for number of cycles to break.

Table I below presents the data which resulted from tests conducted on the coated gut sutures of Examples 2-5 and Comparative Example 1. Tensile strength was tested in accordance with the test procedure described in ASTM D-2256. 20 Percent elongation was tested in accordance with the test procedure described in ASTM D-2256. Young's Modulus, which is a measurement of flexibility, is the initial modulus as determined from the slope of the stress-strain curves produced in straight-pull strength tests carried out in accordance with the test procedure described in ASTM D-2256. Young's Modulus is the ratio of applied stress to strain in the elastic region.

25

Table I

Young's Modulus Example	Number of Cycles to Break	Standard Deviation	Tensile Strength (kpsi)	Percent Elongation (kpsi)
2	52.7	11.0	75	21.3
3	28.4	34.0	76	21
4	17.7	13.0	83	20.5
5	44.5	12.0	81	21.6
Comparative Example 1	0.3	0.2	79.2	18.9
				199.7

40    The number of cycles needed to break each of the sutures of Examples 2-5 and Comparative Example 1 was determined using the fray resistance test schematically illustrated in Fig. 1. A static suture 10 is wound around rollers 12 and tied into a knot 14. A dynamic suture 20 is placed into a grip 23 and extended to reach the static suture 10 where it is wrapped twice at point 25 around the static suture 10. The dynamic suture 20 is extended around roller 26 and attached to a weight 24 which supplies tension to the dynamic suture 20. The grip 23 and dynamic suture 20 move up and down 45 to cause the sutures to rub against each other at point 25. One cycle is a complete up and down movement of the grip 23 and dynamic suture 20. Testing conditions included a preload weight which is 15% of the USP limit on average knot pull strength for gut sutures. The travel distance for the grip was 50mm for each cycle at a speed of 500mm/minute. The test is dependent on the number of cycles needed to break a suture due to the fraying which occurs when one strand of suture, under applied load, slides against another static strand. A modified Sintech 1/G MTS system tester is used 50 to conduct the fraying test. The bottom grip is removed from the tester, the load calibrated and gage set to zero. The static suture 10 is tied with sufficient tension around the rollers 12 of the fixture, forming a square. The fixture is adjusted so the point 25 where the static suture 10 and dynamic suture 20 interface is in line with the center line of the upper grip. The preload weight for these examples was 0.550 (15% of USP knot pull, kg.). The test is initiated with cycling observed until one of the sutures breaks to stop the test. If strands should lock themselves in a knot and do not slide 55 against each other it is considered a break. The average number of cycles ( $X_{ave.}$ ) is  $X_{ave.} = (X_1 + X_2 + \dots + X_n)/n$  wherein  $X_n$  is the number of cycles to break each pair of strands and n is the number of pairs. The standard deviation s is calculated as

$$S = \frac{(x_1 - \bar{x})^2}{n - 1}$$

5 It can clearly be seen from the data of Table I that the average number of cycles to break the dry packaged gut sutures coated in accordance with this disclosure (Examples 2-5) were much higher relative to the uncoated dry packaged gut suture of Comparative Example 1. Furthermore, it can be seen from these data that the tensile strength, percent elongation and Young's modulus of each of the dry packaged coated sutures of Examples 2-5 remained comparable to that of the uncoated dry packaged suture of Comparative Example 1.

10 It will be understood that various modifications may be made to the embodiments disclosed herein. For example, the pre-coating composition can be applied to a gut suture after the bioabsorbable copolymer described herein has been applied to the suture.

The claims which follow identify embodiments of the invention additional to those described in detail above.

15 Claims

1. A gut suture coated with a coating composition comprising a bioabsorbable copolymer obtained by polymerizing a major amount of ε-caprolactone and a minor amount of at least one other copolymerizable monomer in the presence of polyhydric alcohol as initiator.
2. The gut suture of Claim 1 wherein the other copolymerizable monomer is selected from glycolide, lactide, p-dioxanone and trimethylene carbonate.
3. The gut suture of Claim 1 wherein the polyhydric alcohol initiator is selected from glycerol, trimethylolpropane, 1,2,4-butanetriol, 1,2,6-hexanetriol, triethanolamine, triisopropanolamine, erythritol, threitol, pentaerythritol, ribitol, arabinitol, xylitol, N,N,N',N'-tetrakis(2-hydroxyethyl)ethylenediamine, N,N,N',N'-tetrakis(2-hydroxypropyl)ethylenediamine, dipentaerythritol, allitol, dulcitol, glucitol, altritol, iditol, sorbitol, mannitol and inositol.
4. The gut suture of Claim 1, 2 or 3 wherein the copolymer contains from about 70 to about 98 weight percent ε-caprolactone-derived units, the balance of the copolymer being derived from the other copolymerizable monomer(s).
5. The gut suture of Claim 4 wherein the copolymer contains from about 80 to about 95 weight percent ε-caprolactone-derived units, the balance of the copolymer being derived from the other copolymerizable monomer(s).
- 35 6. The gut suture of any one of the preceding claims wherein the copolymer possesses an inherent viscosity of from about 0.10 to about 0.60 dl/g when measured in chloroform at a concentration of 0.2500 g/dl at 30°C.
7. The gut suture of any one of the preceding claims wherein the copolymer possesses a molecular weight of from about 0.20 to about 0.50 dl/g when measured in chloroform at a concentration of 0.2500 dl/g at 30°C.
- 40 8. The gut suture of any one of the preceding claims wherein the polyhydric alcohol initiator is employed in an amount of from about 0.5 to about 5 weight percent of the total monomer mixture.
9. The gut suture of any one of claims 1 to 7 wherein the polyhydric alcohol initiator is employed in an amount of from about 0.1 to about 2 weight percent of the total monomer mixture.
- 45 10. The gut suture of any one of the preceding claims wherein the coating composition is applied to a gut suture at a level of from about 0.2 to about 4 weight percent of the entire coated suture.
11. The gut suture of Claim 10 wherein the coating composition is applied to a gut suture at a level of from about 0.5 to about 3 weight percent of the entire coated suture.
- 50 12. The gut suture of any one of the preceding claims wherein the suture is precoated with a pre-coating composition comprising fatty acids, esters and ethers of fatty acids, polyalcohols, fatty alcohols, glycerine, glycols and derivatives thereof and poly(alkylene oxides) prior to application of the coating composition.
13. The gut suture of Claim 12 wherein the pre-coating composition comprises a poly(alkylene oxide) selected from polyethylene glycol, polypropylene glycol and polyethylene glycol methyl ether.

14. The gut suture of Claim 13 wherein the poly(alkylene oxide) possesses a molecular weight which ranges from about 300 to about 5000.
15. The gut suture of any one of the preceding claims wherein the suture is dry packaged.

5

10

15

20

25

30

35

40

45

50

55

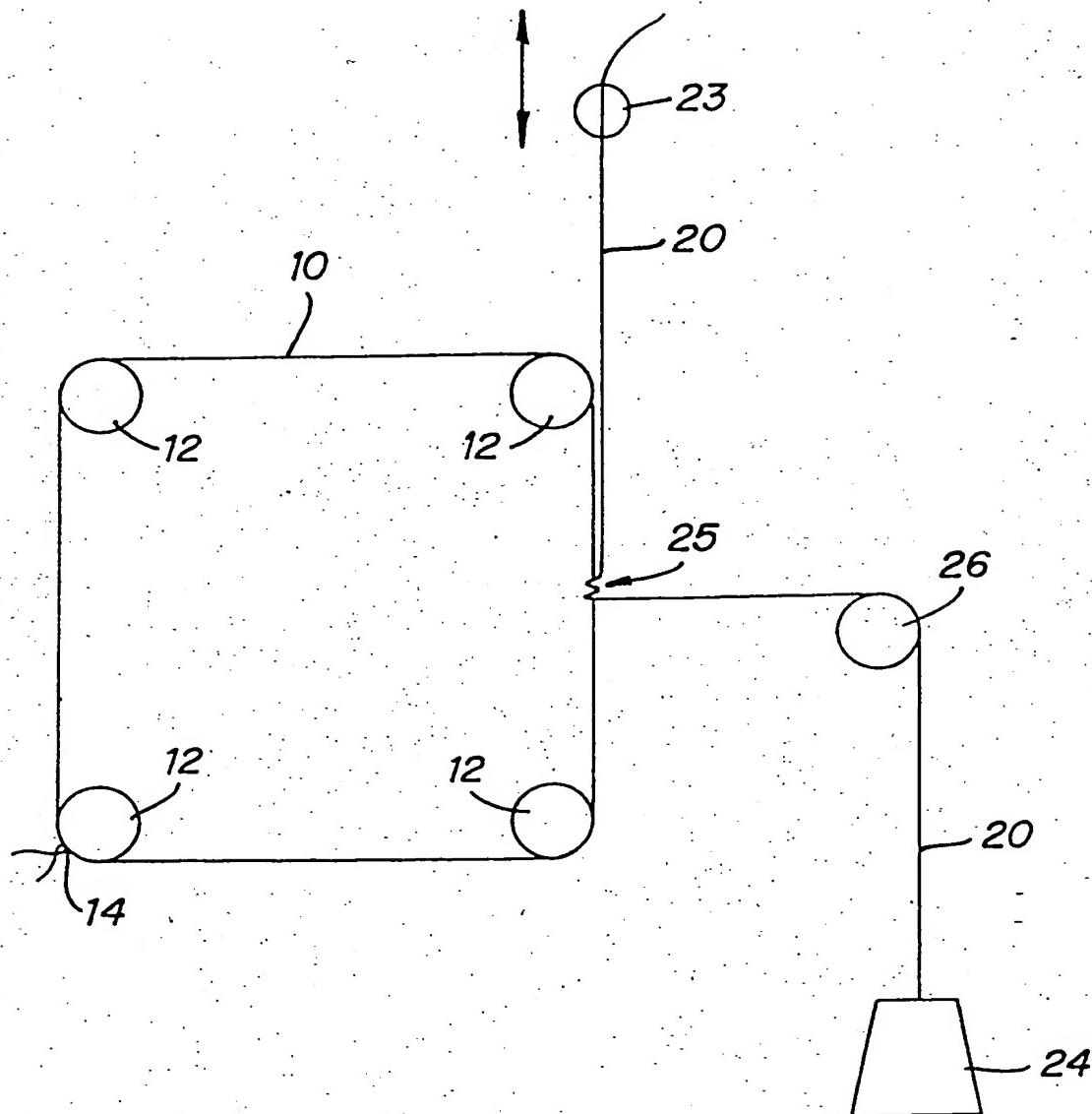


FIG. 1



European Patent  
Office

## EUROPEAN SEARCH REPORT

Application Number

EP 95 11 8169

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	EP-A-0 628 587 (UNITED STATES SURGICAL CORP) 14 December 1994 * page 2, line 35 - page 3, line 26; claims 7-9; examples *	1-15	A61L17/00
Y	US-A-5 037 429 (HERMES MATTHEW E ET AL) 6 August 1991 * column 3, line 52 - column 4, line 14 * * column 5, line 33 - line 46 *	12-15	
Y,D	US-A-3 896 814 (VIVIEN DANIEL ET AL) 29 July 1975 * column 2, line 16 - line 32; example 3 *	12-15	
A	EP-A-0 128 043 (ETHICON INC) 12 December 1984		
A	US-A-4 201 216 (MATTEI FRANK V) 6 May 1980 * claims *	12	
			TECHNICAL FIELDS SEARCHED (Int.Cl.)
			A61L
<p>The present search report has been drawn up for all claims</p>			
Place of search	Date of completion of the search	Examiner	
THE HAGUE	22 April 1996	Cousins-Van Steen, G	
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : ooo-written disclosure P : intermediate document			
T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			